Isolator Design and Air handling

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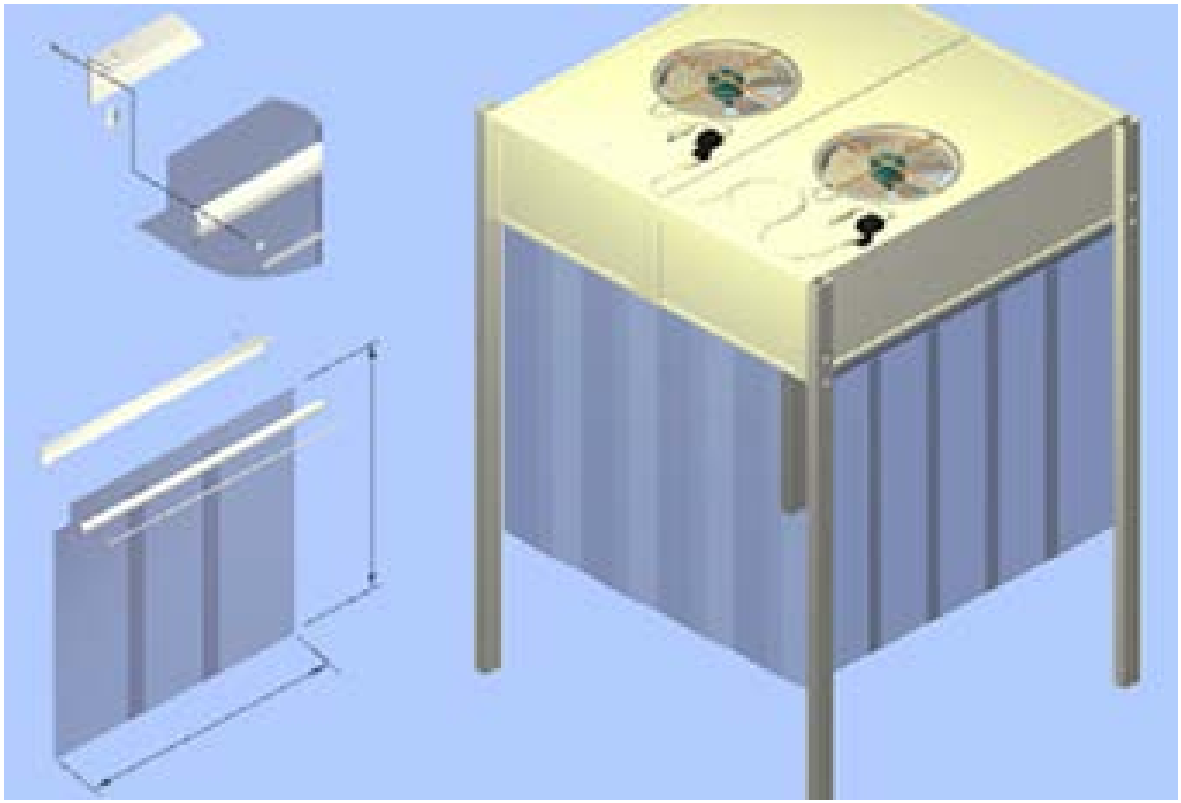
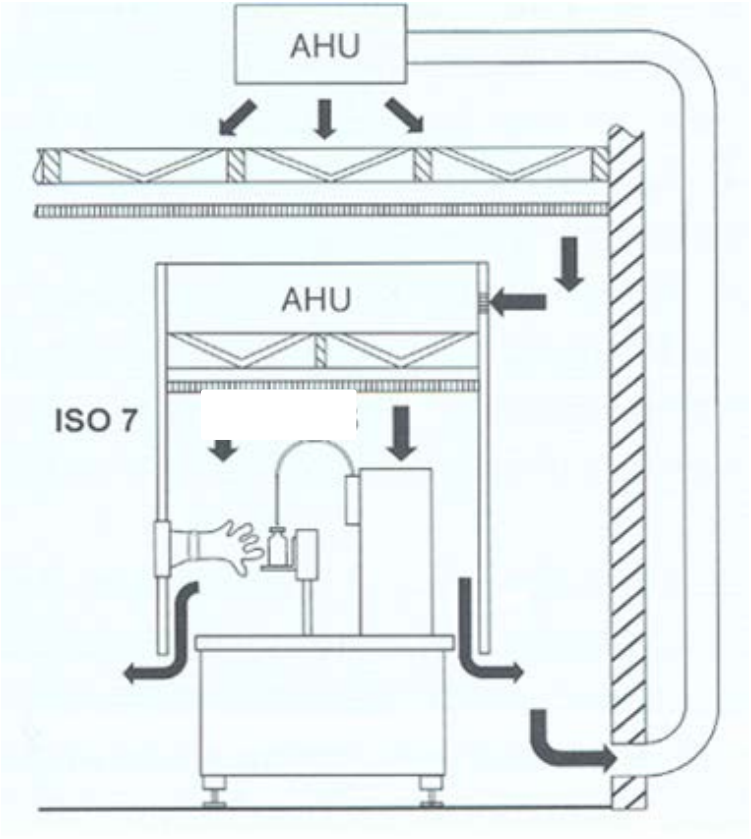
Conventional technology
v.s
Isolator

Clean booth



Room:	Grade B
SLR (SAL):	3
Laminar flow:	Yes
Pressure control	No
Leak tight design	No
Decontamination	No
Glove access	No

•Open RABS



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Laminar flow:	Yes
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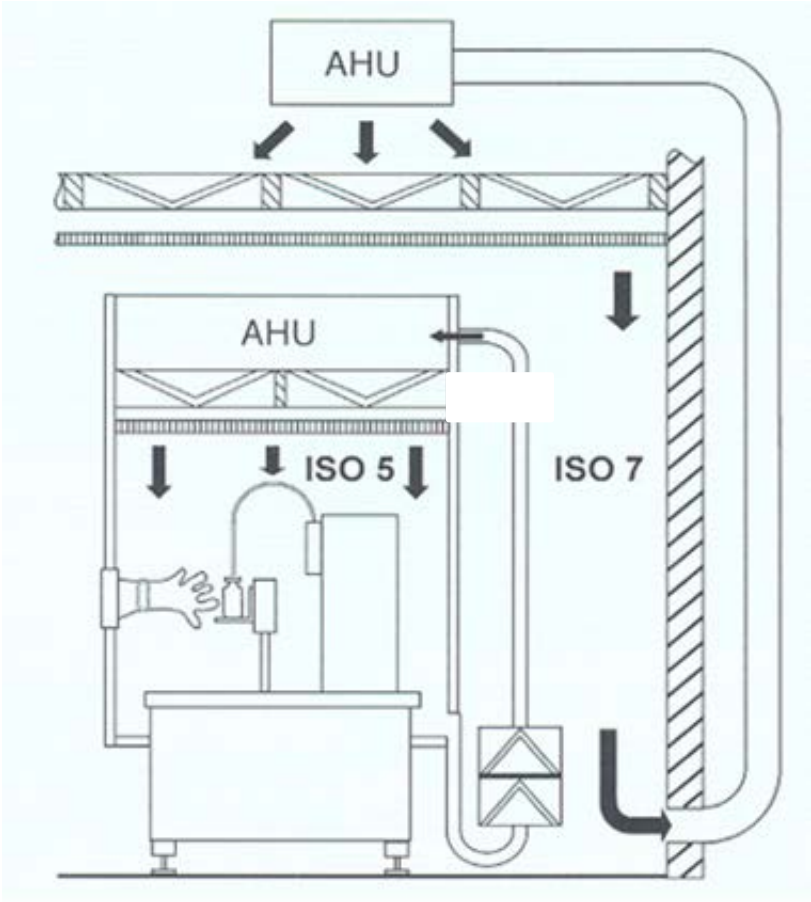
Glove access	Yes

•Closed RABS



Room:	Grade B
SLR (SAL):	3
Laminar flow:	Yes
Pressure control	Yes
Leak tight design	30 to 40%/vol/h
Decontamination	No
Glove access	Yes

No. of recalls of sterile drugs in Australia and their source 2012 ~ 2014

	Risk of non sterile	Foreign Particles (possible risk of contamination)	Total no. of recalls (only Injections)	Ratio between sterile risk recalls and total no.
2014	3	2	10	50%
2013	3	1	22	18%
2012	1	0	11	9%
US in 2014	3	2	NA	NA

* Data from TGA SARA

Main reason why no. of recalls based on non-sterile risk are stable is…

Conventional clean room technology!!

3 Risks of contamination caused by clean room technology

1) No pressure control
2) No decontamination
3) SLR (SAL)3

Room:	Grade B
SLR (SAL):	3
Laminar flow:	Yes
Pressure control	No
Leak tight design	No
Decontamination	No
Glove access	Yes

•Isolator as process

We need ultimate solution which can cover 3 Risks of contamination caused by conventional clean room technology

1) No pressure control

=> Pressure control

Solution => SS wall and Visual through glass and glove access

2) No decontamination

=> Decontamination function to actively create aseptic environment

Solution => H2O2 decontamination

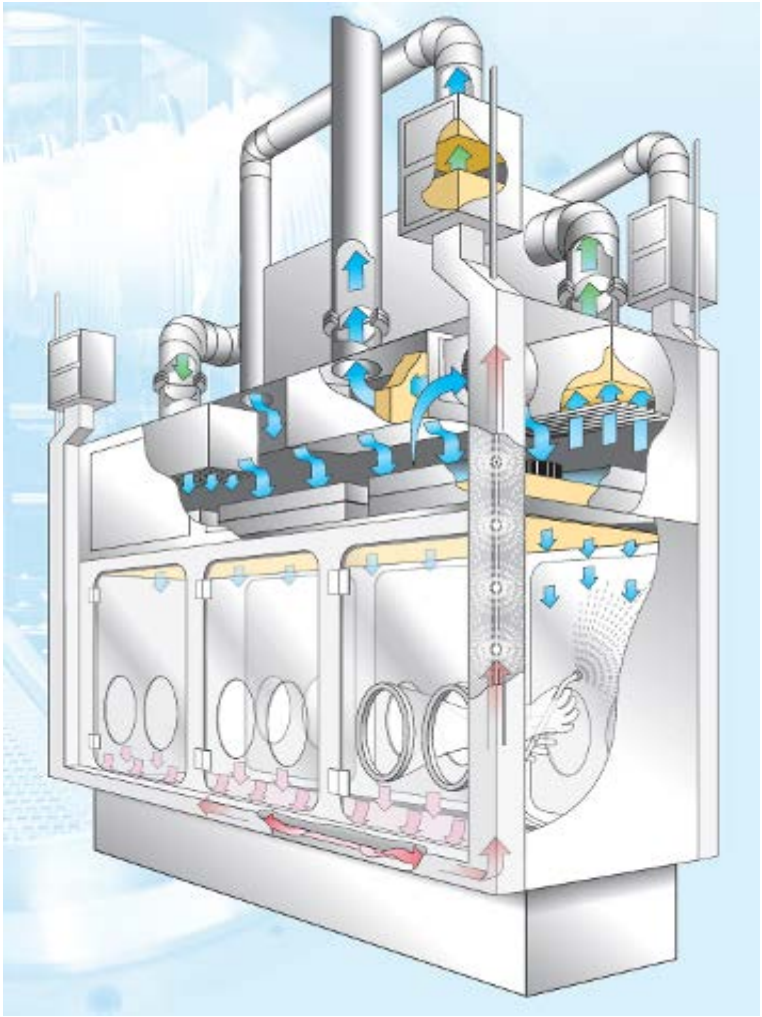
3) SLR (SAL3)

=> SLR (SAL6)

Solution => H2O2 decontamination and daily program

Therefore the isolator must consists of…

•Isolator



Room:	Grade C/D
SLR (SAL):	6
Laminar flow:	Yes
Pressure control	Yes
Leak tight design	Yes down to 1%
Decontamination	Yes
Glove access	Yes

Definition of Isolator

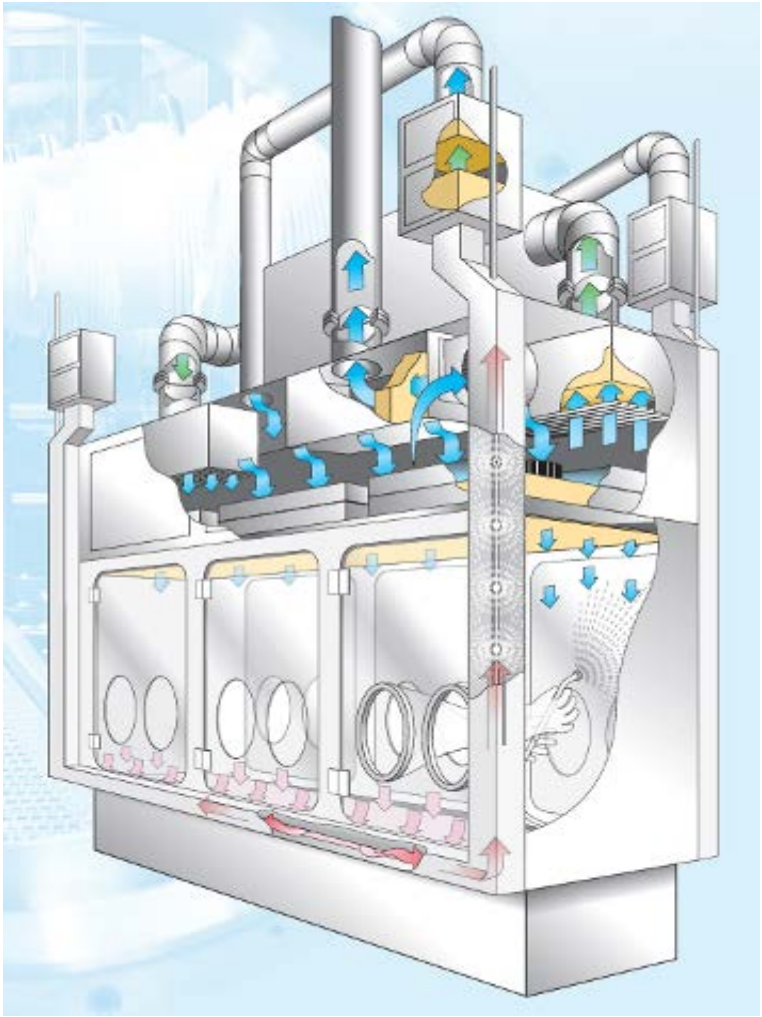
2. INTRODUCTION

2.1 The term 'Isolator' as used in the Pharmaceutical Industry covers a variety of pieces of equipment. One group has the main objective of providing containment for the handling of dangerous materials either aseptically or not. Another group has the main objective of providing a microbiologically controlled environment within which aseptic operations can be carried out.

Containment isolators often employ negative internal air pressure and most isolators used for aseptic processing employ positive pressure. A sporicidal process, usually delivered by gassing, can be used to aid microbiological control. Some large scale isolators provide an opening, often called a mousehole, to permit continuous removal of sealed product. Other isolators remain sealed throughout production operations. The capability for the isolator to be sealed allows operations to be carried out in controlled gaseous environments e.g. anaerobic conditions.

* PICs Isolators Used for Aseptic Processing and Sterility Testing

•Isolator



Room:	Grade C/D
SLR (SAL):	6
Laminar flow:	Yes
Pressure control	Yes
Leak tight design	Yes down to 1%
Decontamination	Yes
Glove access	Yes

Major functions of isolator

Air Tightness	Critical zone	Qualification and Documents
Differential pressure Control	Decontamination and Daily program	Monitoring / Alarm
FIlters	Machines	Operator Training
AHUs	Aseptic transfer	Maintenance
Surrounding room	Cleaning	Sub components

Air Tightness

Decision process of isolator leak rate

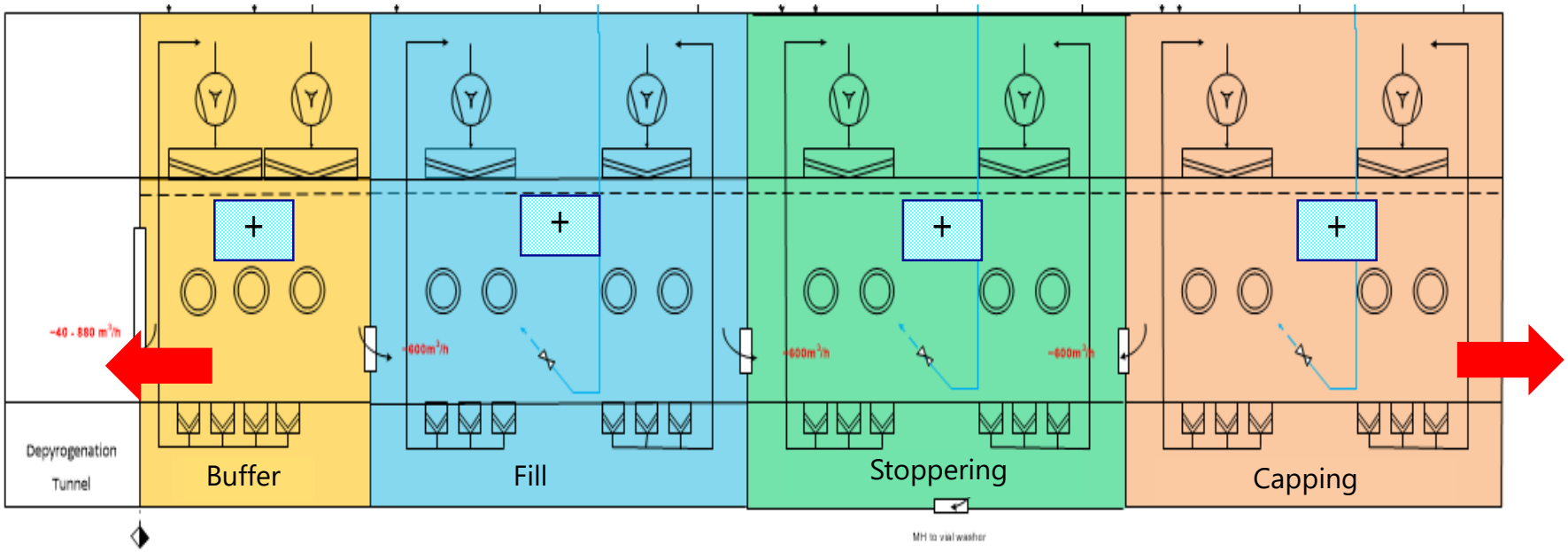
Guideline (Internal and external)

Pos	Title	Dokumenten ID	
1	Analyse der GMP Anforderungen an Isolatorsysteme	4-04-800-013513A04	Outline Isolator Analysis (GMP)
2	ISO 10648-2(1994) Containment enclosures – part2: classification according to leak tightness and associated checking methods.	ISO 10648-2(1994)	ISO Containment Leak test method
3	Risikoanalyse Isolatorsysteme	015287_A	Isolator system risk analysis
4	Risikoanalyse SIS 700	015293_A	Risk analysis SIS700
5	Erlass der Schweizerrischen Unfallversicherungsanstalt SUVA Grenzwerte am Arbeitsplatz 2003	SUVA; 1903.d	Swiss accident insurance Limitation for work station
6	Power Point Presentation H2O2 gas Concentration Measurement	VSI, 31.03.2004	H2O2 gas concentration measurement
7	A validated Calibration Method for Hydrogen Peroxide Gas	PDA Journal, Vol.55, No.1, Jan./Feb.2001	H2O2 sensor calibration method
8	Theoretical Analysis of the Condensation of Hydrogen Peroxide Gas and Water Vapour as Used in Surface Decontamination	PDA Journal, Vol.56, No.6, Nov./Dec.2002	Distribution of H2O2 gas
9	Application of a Newly Developed Hydorogen Peroxide Vapour Phase Sensor to HPV Sterilizer	PDA Journal, Vol.52, No.1, Jan./Feb.1998	Use of H2O2 sensor
10	Dichtigkeitsberechung von Isolatoren	Excel Tabellen Kalkulation	Calculation of isolator leak

Complex Pressure Control of
Fill Finish Production Isolators
(aseptic and aseptic/toxic)

Pressure

Vial line (aseptic only)

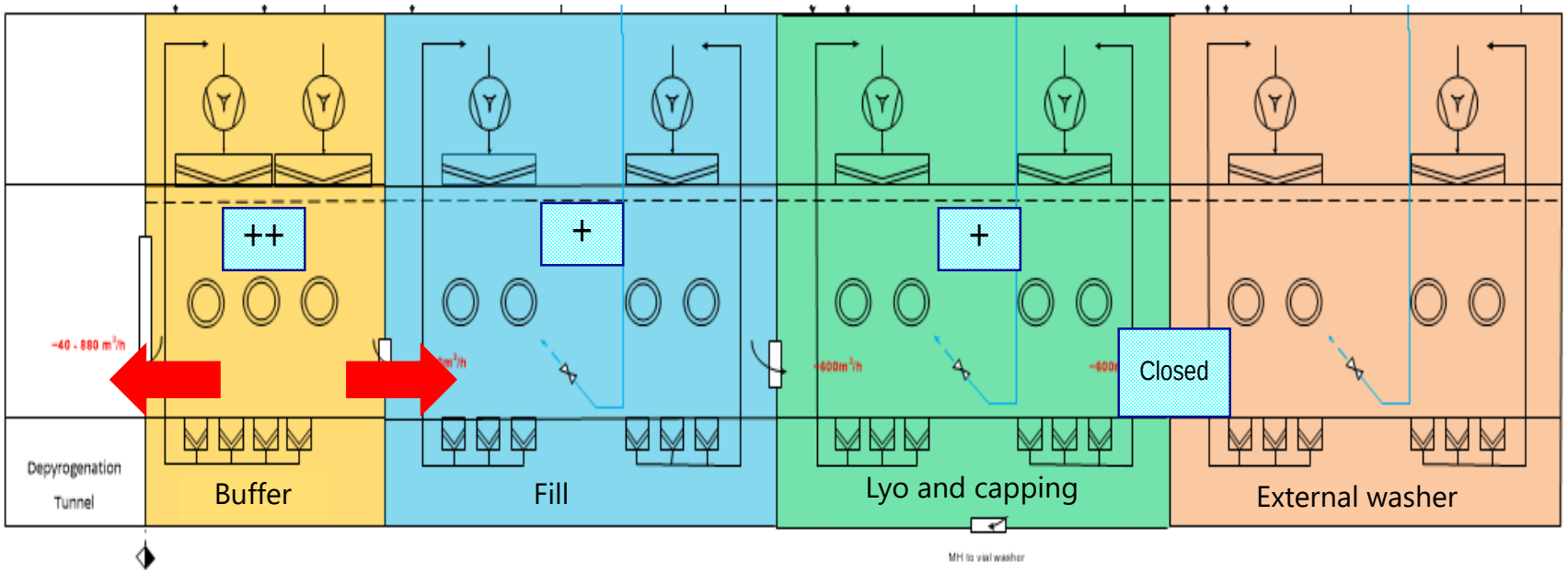


Air Flow (by design, depending on phase)

Design for Primary Containment

Reduce potential spreading – pressure control

Fill to lyophilize loading



Air Flow (by design, depending on phase)

Air Handling goes to GREEN.

Area for AHU and Electrical Panels

Thank you